underlying bleeding mechanism for viral hemorrhagic fever is complex, possible factors include thrombocytopenia alone, thrombocytopenia associated with disseminated intravascular coagulation, endothelial cell dysfunction, or decreased coagulation factor levels in plasma. Prior to Applicants discovery, no effective therapy for treating viral hemorrhagic fever existed and, absent viral-specific chemotherapy, management was primarily supportive. Applicants discovered that human patients suffering from viral hemorrhagic fever could be treated with human protein C zymogen. In particular, protein C - which includes human protein C zymogen - with its anticoagulant, anti-inflammatory, and profibrinolytic activities is useful for treatment of the hypercoagulable state or protein C deficiency that occurs in viral hemorrhagic fever patients.

Claim 1 is pending in this case.

REJECTION OF CLAIM 1 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claim 1 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully assert that the invention is fully enabled and request withdrawal of this rejection.

The examiner initially asserts that Applicants "clearly admitted that the instant invention is directed to treatment of viral hemorrhagic fever with activated protein C, not with its zymogen" on page 6 of the disclosure. Applicants respectfully point out to the Examiner that the disclosure on page 6 is part of a definition for r-aPC (recombinant human activated protein C). As such, the definition describes - among the various means for obtaining r-aPC - the secretion of the zymogen from human kidney 293 cells and its subsequent

purification and activation. This disclosure does not in any way "clearly admit" that the invention is directed to treatment of viral hemorrhagic fever with activated protein C at the exclusion of human protein C zymogen. In further support of this point, Applicants direct the Examiner's attention to definitions for protein C, zymogen, HPC, and r-hPC on page 5 of the disclosure. These definitions illustrate that Applicants included human protein C zymogen and activated protein C within their disclosure. Furthermore, the term 'protein C' - as used in this specification - reasonably includes both activated protein C and the human protein C zymogen. More particularly, on page 8 of the disclosure, Applicants describe protein C for numerous aspects of the current invention including 1) the treatment of viral hemorrhagic fever, 2) a particular formulation including protein C, 3) administration by continuous infusion for a predetermined period of time, and 4) a particularized dosage range. Since the teachings on page 8 are related to the person skilled in the art in terms that distinguish protein C from activated protein C (e.g. lines 11 through 12: protein C or aPC; lines 23 through 25: the protein C used . . . is activated protein C (aPC)), the term protein C is reasonably understood therein to teach the use of human protein C zymogen. Plus, the suggested quantities and means of administration throughout the disclosure are directed to activated protein C and/or protein C, depending on the particular section. As such, the zymogen is fairly included in any of Applicants' teachings involving protein C. Given these points, Applicants assert that the invention is enabled so to use human protein C zymogen to treat patients suffering from viral hemorrhagic fever.

Additionally, the Examiner points out, and Applicants agree, that the example noted in the disclosure regarding patients' treatment of viral hemorrhagic fever uses

recombinant human activated protein C and not the zymogen. However, as noted above, the disclosure involves protein C - thereby including the zymogen - and not activated protein C alone. Applicants also respectfully point out that under MPEP 2164.02, compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. Furthermore, the specification does not need to contain an example if the invention is disclosed so that one skilled in the art can practice it without undue experimentation. *See* MPEP 2164.02 and *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Here, Applicants disclose teachings regarding the use of protein C for the treatment of viral hemorrhagic fever along with a particularized dosage level, an administration means and duration, and a formulation. Thus, the lack of an example in the disclosure using the zymogen does not foreclose enablement.

The Examiner also looks to Bang et al. (U.S. 5,151,268) to show that the zymogen is activated *in vivo* very slowly due to the thrombin required for activation. The activation rate, while slow, does not mean that the zymogen does not work or that the claims lack enablement due to the slow activation rate. Indeed, Applicants' disclosure teaches that the zymogen treats viral hemorrhagic fever as well as a specific dosage range for using the zymogen in that manner. These teachings provide the skilled artisan with the information necessary to avoid undue experimentation. For these as well as the other above-stated reasons, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants discovered an important, previously unknown method for treating patients suffering from viral hemorrhagic fever using human protein C zymogen. The

invention further claims a particularized dose, administration by continuous infusion for a particular time period, and a formulation. As such, Applicants have provided a disclosure that enables one skilled in the art to make and/or use the invention.

In view of these points, Applicants courteously solicit reconsideration of the rejection and passage of this case to issuance.

Respectfully submitted,

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